

What is claimed is:

1.

A method for delivering a biological agent to specific tissue sites comprising:
forming a solution of a plurality of protein encapsulated, insoluble gas-filled microbubbles, said microbubbles conjugated to said biological agent;
administering said solution to an animal; so that said protein directs the microbubble-conjugated agent to sites of bioprocessing of said protein and upon dissipation of the microbubble releases said agent.

2.

The method of claim 1 wherein said microbubbles are formed under conditions which lower the partial pressure of nitrogen within the microbubble compared to the partial pressure achieved with room air sonication.

3.

The method of claim 1 wherein said microbubbles are formed in a nitrogen free environment.

4.

The method of claim 3 wherein said environment consists of oxygen.

5.

The method of claim 1 wherein said protein is selected from the group consisting of albumin, human gamma, globulin, human apotransferin, beta lactose and urease.

6.

The method of claim 1 wherein said protein is albumin.

7.

The method of claim 1 wherein said insoluble gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, and perfluoropentane.

8.

The method of claim 7 wherein said gas is perfluoropropane.

9.

The method of claim 1 wherein said microbubbles are formed by the steps of:
mixing an aqueous solution comprising about 2% to about 10% by weight of human serum albumin diluted about two-fold to about eight-fold with 5% to 50% by weight of dextrose; and
exposing said solution to a sonication horn in a nitrogen-free environment to create cavitation at particulate sites in said solution thereby generating stable microbubbles from about .1 to 10 microns in diameter.

10.

The method of claim 9 wherein said dilution of albumin with dextrose is a three-fold dilution.

11.

The method of claim 9 wherein said human serum albumin is a 5% by weight solution.

12.

The method of claim 9 wherein said dextrose is a 5% by weight solution.

13.

The method of claim 9 wherein said protein is albumin and said biological agent is selected from the group consisting of: an oligonucleotide, a polynucleotide, a ribozyme, naproxen, piroxicam, warfarin, furosemide, phenylbutazone, valproic acid, sulfisoxazole, ceftriaxone, miconazole.

14.

The method of claim 13 wherein said biological agent is an oligonucleotide.

15.

The method of claim 14 wherein said oligonucleotide is a phosphorothioate oligonucleotide.

16.

The method of claim 15 wherein said phosphorothioate oligonucleotide is an antisense oligonucleotide.

17.

The method of claim 9 wherein the solution is exposed to a nitrogen-free environment comprising 100% oxygen.

18.

The method of claim 17 wherein the 100% oxygen is blown into interface between the sonicating horn and the solution.

19.

The method of claim 9 wherein said target site is the liver and the kidney of said animal.

20.

A microbubble composition for ultrasonic imaging or for delivery of a biological agent to a target site comprising:

an aqueous suspension comprising a plurality of protein encapsulated insoluble gas-filled microbubbles, wherein the partial pressure of nitrogen in said bubbles is decreased compared to the partial pressure of nitrogen in room air sonicated microbubbles.

21.

The composition of claim 20 wherein said gas-filled microbubbles are nitrogen free.

22.

The composition of claim 20 wherein said protein is selected from the group consisting of albumin, human gamma globulin, human apotransferin, beta lactose and urease.

23.

The composition of claim 20 wherein said protein is albumin.

24.

The composition of claim 20 wherein said gas is a perfluorocarbon gas.

25.

The composition of claim 20 wherein said gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, and perfluoropentane.

26.

The composition of claim 20 wherein said gas is perfluorobutane.

27.

The composition of claim 20 wherein said gas is perfluoropropane.

28.

The composition of claim 20 wherein said protein is albumin and said biological agent is selected from the group consisting of: an oligonucleotide, a polynucleotide, a ribozyme, naproxen, piroxicam, warfarin, furosemide, phenylbutazone, valproic acid, sulfisoxazole, ceftriaxone, miconazole.

29.

The composition of claim 28 wherein said biological agent is an oligonucleotide.

30.

The composition of claim 22 wherein said gas-filled microbubbles comprise 100% pure oxygen.

31.

A composition for delivery of nucleotide based biological agents to a target site comprising:
a plurality of albumin encapsulated insoluble gas-filled microbubbles, wherein the gas filling the microbubbles is nitrogen-free; and
a nucleotide based biological agent conjugated to said albumin microbubbles.

32.

The composition of claim 31 wherein said microbubbles are .1 to 10 microns in diameter.

33.

The composition of claim 31 wherein said gas is a perfluorocarbon gas.

34.

A method for delivering nucleotide based biological agents to the kidney and liver of animals comprising: forming a solution comprising a plurality of albumin encapsulated insoluble gas-filled microbubbles, said microbubbles conjugated to said nucleotide based biological agent; and administering said solution to an animal; so that said albumin encapsulated microbubble is taken up by said liver and said kidney and upon dissipation of the microbubble, releases said biological agent.

35.

The method of claim 34 wherein said nucleic acid biological agent is selected from the group consisting of an antisense oligonucleotide, antigene oligonucleotide, oligonucleotide probe, or a nucleotide vector.

36.

The method of claim 34 wherein said gas filling said microbubbles is nitrogen free.